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Abstract: **OBJECTIVES:** To treat aortic valve disease and concomitant root disease with transcatheter techniques, 'composite graft' implants are required. Our goal was to assess the suitability of the porcine aortic root for transcatheter root repair tests. **METHODS:** Eight pig hearts explanted from domestic pigs used in experimental surgery were compared to data from the literature on human hearts. The measured diameters included those of the annulus, sinuses of Valsalva, coronary ostia, sinotubular junction, ascending aorta, innominate artery and aortic arch. The measured distances were from the coronary ostia to the nadir of the corresponding annulus; from the innominate artery to the nadir of the corresponding annulus; from the small curvature of the arch to the nadir of the corresponding annulus. **RESULTS:** The mean weight of the pigs was 89 ± 5.4 kg. The mean aortic annulus diameter was 20 ± 1.2 mm (human: 23.0 ± 2.5 mm), the sinus of Valsalva diameter was 20.5 ± 0.5 mm (human: 31.4 ± 3.4 mm) and the sinotubular junction diameter was 20 ± 0.9 mm (human: 27.2 ± 3.0 mm). The diameter of the mean ascending aorta was 19 ± 0.7 mm (human: 29.3 ± 4 mm); the diameter of the innominate artery was 8.5 ± 0.7 mm, that of the aortic arch was 15 ± 0.7 mm and that of the coronary ostia was 5 ± 0.5 mm (left) and 4.7 ± 0.5 mm (right) (human: 4.8 ± 0.5 mm and 3.7 ± 0.9 mm). The distances from the left and right coronary orifices to the corresponding annuli were 8 ± 1.5 mm and 14 ± 2.4 mm, respectively (human: 14.7 ± 1.3 mm; 15.4 ± 1.7 mm). The distances from the innominate artery to the nadirs of the left and right coronary annuli were 44 ± 4.3 mm and 41 ± 4 mm (human: 80 ± 17 mm). The distance from the curvature of the small arch to the annulus was 35 ± 4.9 mm. **CONCLUSIONS:** The porcine heart can be used as an experimental model to design and test new devices for catheter-based composite repair of the aortic root. Nevertheless, caution is required in using devices with tailored dimensions that must be adapted to the smaller pig's root.

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Suitability of the porcine aortic model for transcatheter aortic root repair

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Abstract

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METHODS: Eight pig hearts explanted from domestic pigs used in experimental surgery were compared to data from the literature on human hearts. The measured diameters included those of the annulus, sinuses of Valsalva, coronary ostia, sinotubular junction, ascending aorta, innominate artery and aortic arch. The measured distances were from the coronary ostia to the nadir of the corresponding annulus; from the innominate artery to the nadir of the corresponding annulus; from the small curvature of the arch to the nadir of the corresponding annulus.

RESULTS: The mean weight of the pigs was 89 ± 5.4 kg. The mean aortic annulus diameter was 20 ± 1.2 mm (human: 23.0 ± 2.5 mm), the sinus of Valsalva diameter was 20.5 ± 0.5 mm (human: 31.4 ± 3.4 mm) and the sinotubular junction diameter was 20 ± 0.9 mm (human: 27.2 ± 3.0 mm). The diameter of the mean ascending aorta was 19 ± 0.7 mm (human: 29.3 ± 4 mm); the diameter of the innominate artery was 8.5 ± 0.7 mm, that of the aortic arch was 15 ± 0.7 mm and that of the coronary ostia was 5 ± 0.5 mm (left) and 4.7 ± 0.5 mm (right) (human: 4.8 ± 0.5 mm and 3.7 ± 0.9 mm). The distances from the left and right coronary orifices to the corresponding annuli were 8 ± 1.5 mm and 14 ± 2.4 mm, respectively (human: 14.7 ± 1.3 mm; 15.4 ± 1.7 mm). The distances from the innominate artery to the nadirs of the left and right coronary annuli were 44 ± 4.3 mm and 41 ± 4 mm (human: 80 ± 17 mm). The distance from the curvature of the small arch to the annulus was 35 ± 4.9 mm.

CONCLUSIONS: The porcine heart can be used as an experimental model to design and test new devices for catheter-based composite repair of the aortic root. Nevertheless, caution is required in using devices with tailored dimensions that must be adapted to the smaller pig’s root.

Keywords: Aortic root • Ascending aorta • Porcine heart • Transcatheter aortic root repair

INTRODUCTION

Ascending aorta and aortic root diseases are potentially life-threatening and require prompt medical and surgical treatment. Surgery is the most valuable therapeutic option to prevent adverse events and to save lives in the case of dissections, aneurysms, pseudoaneurysms, haematomas or penetrating ulcers. However, despite the low mortality rate and the good long-term results of standard surgery, complications and deaths are higher in elderly patients or in those with severe concomitant comorbidities.

Recent reports showed that elective replacement of the proximal aorta has an overall hospital mortality rate of approximately

4% that increases up to 7.9% for patients aged 70 years or more [1]. Therefore, catheter-based techniques are coming into prominence as alternative minimally invasive treatments. Recently, they have been applied in selected cases of non-dissected ascending aorta disease or ascending aorta dissection [2].

However, technical and anatomical difficulties in the proximal aortic segments make the treatment of aortic root diseases (e.g. aortic root aneurysm) more challenging with the available catheter-based techniques and technologies. Additionally, in the case of combined aortic root and aortic valve disorders, a ‘composite-graft’ implant for transcatheter root and valve replacement is required.

To use the porcine heart as an experimental model for the development and testing of these new devices, it is important to study the anatomy of the root and of the ascending aorta in pigs (adult domestic pigs available in animal laboratories). Surprisingly, despite its importance as an experimental model for many of the recently developed intracardiac devices and technologies, the available information on this porcine anatomical part is limited [3].

The present study was designed to assess the suitability of the porcine aorta for transcatheter root repair (which by definition includes the valve) and to provide the morphological basis for the design of new devices and technologies for future transcatheter aortic root repairs.

METHODS

We analysed 8 fresh porcine hearts that were harvested from healthy domestic pigs donated post-mortem by the animal laboratory of the University Hospital of Zurich (Switzerland). All hearts that included the aortic root, the ascending aorta and the aortic arch were obtained from healthy animals that had no recognizable congenital or acquired cardiovascular diseases. These animals had been previously used in other studies with experimental protocols approved by the Cantonal Veterinary Department of Zurich, Switzerland (license No. ZH 152/2013, in accordance with the Swiss Animal Protection Law). Housing and experimental procedures also conformed to both the European Directive 2010/63/EU of the European Parliament and of the council on the protection of animals used for scientific purposes, and the Guide for the Care and Use of Laboratory Animals (Institute of Laboratory Animal Resources, National Research Council, National Academy of Sciences, 2011).

Specimen preparation

All specimens were fresh (not frozen), and no chemical fixation was applied. The specimens were prepared and measured by a cardiac surgeon. After they were extracted from the pigs' bodies, the specimens were washed, weighed, dissected and measured. All hearts were normal (no congenital heart defects were observed). Each specimen was harvested *en bloc* including the heart, the ascending aorta and the full aortic arch with the innominate artery. The aorta was transected at the level of the proximal descending aorta. The aortic root was dissected free from the surrounding cardiac structures, similarly to the valve-sparing reimplantation technique. The innominate artery and coronary arteries were fully dissected (Fig. 1A).

Specimen measurements

The weights of the donors and the hearts were recorded. We measured 13 parameters of the aortic root and ascending aorta: the annulus diameter, the diameter of the sinuses of Valsalva, the diameters of the left and right coronary arteries, the diameter of the sinotubular junction (STJ), the diameter of the middle portion of the ascending aorta, the diameter of the innominate artery, the diameter of the aortic arch, the distance from the left and right coronary ostia to the nadir of the corresponding annulus, the distance from the innominate artery ostia to the nadir of the left and right corresponding annuli and the distance from the start of the small curvature of the aortic arch to the nadir of the annulus.

The specimens were held in place to maintain a normal anatomical configuration without additional tension on the tissues. The measurements were taken with a point compass and a ruler. For each animal heart, every measurement was performed 3 times by 2 different operators, and the mean was taken as the result. The diameters of the arteries were measured from the inner opposite sides of the arterial walls (Fig. 1B). Then, the aortic root and the left ventricular outflow tract were opened longitudinally in the middle of the anterior mitral leaflet and between the left coronary and the non-coronary aortic valve leaflets (Fig. 1C). The diameters of the aortic annulus, sinuses of Valsalva, STJ and of the middle portion of the ascending aorta were measured from their circumference divided by π ($d = C/\pi$; d = diameter; C = circumference; $\pi = 3.14$). The diameters of the coronary ostia, aortic arch and innominate artery were measured from one inner side of the aortic wall to the other inner side with the compass (Fig. 1B). The distance from the left and right coronary ostia to the nadir of the corresponding annulus, the distance from the origin of the innominate artery to the nadir of the left and right corresponding annuli and the distance from the start of the small curvature of the aortic arch to the nadir of the annulus were taken with direct measurements (Fig. 1D).

Human data

For comparison, we searched the available literature for data on the human aortic root, ascending aorta, coronary ostia and aortic arch and compared the information we found to the measured data obtained from the animal specimens [4–14]. Measurements of the human heart were obtained *in vivo* from echocardiograms or computed tomography scans of pressurized aortas.

Statistical analysis

Data from animal specimens were collected and organized on an Apple Numbers spreadsheet (version 6.6.2). Descriptive statistics with mean values and standard deviations (mean \pm standard deviation) were used to describe the collected continuous variables.

RESULTS

None of the dissected hearts showed signs of congenital or acquired disease. The mean weights of the 8 animal donors (all female) and their hearts were 89 ± 5.4 kg and 361 ± 44.5 g, respectively. Data on the human heart and aorta were obtained from the published literature [4–14].

As in the human heart, in the porcine heart, the aortic root extends from the left ventricular outflow tract to the ascending aorta and encompasses 4 anatomical structures: the aortic annulus, the aortic valve cusps, the aortic sinuses (sinuses of Valsalva) and the STJ (Fig. 1C). The aortic valve has 3 leaflet cusps, and each cusp has a semilunar shape.

Hereafter, anatomical data from human hearts taken from the literature are given in parentheses, where available. The mean diameters of the aortic annulus, the sinuses of Valsalva and the STJ were 20 ± 1.2 mm, 20.5 ± 0.5 mm and 20 ± 0.9 mm (23.0 ± 2.5 mm, 31.4 ± 3.4 mm, 27.2 ± 3.0 mm in human hearts), respectively. The mean diameters of the ascending aorta, innominate artery and

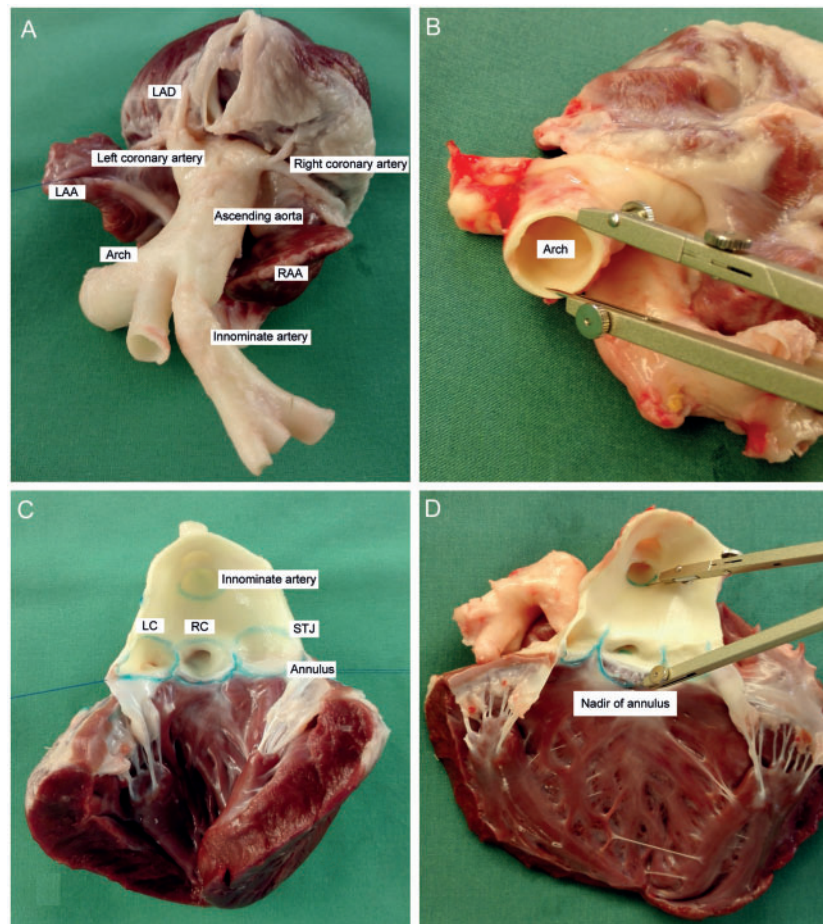


Figure 1: (A) The whole porcine heart showing the aortic root, coronary arteries, ascending aorta, innominate artery and arch from the outside. (B) The diameters of the innominate artery and the arch were taken from the inner side of the arterial wall. (C) The open aortic root. (D) The distance from the origin of the innominate artery to the nadir of the right coronary annulus. LAA: left atrial appendage; LAD: left anterior descending; LC: left coronary; RAA: right atrial appendage; RC: right coronary; STJ: sinotubular junction.

aortic arch were 19 ± 0.7 mm (in human hearts 29.3 ± 4 mm), 8.5 ± 0.7 mm and 15 ± 0.7 mm, respectively. Compared to the human heart, the porcine heart has only 2 head branches that originate from the arch. The distance from the origin of the right innominate artery to the nadir of the left and right annuli was 44 ± 4.3 mm and 41 ± 4 mm, respectively (in human hearts, the distance was 80 ± 17 mm). The distance from the start of the small curvature of the arch to the nadir of the annulus was 35 ± 4.9 mm.

As in the human heart, the porcine coronary arteries arise from their respective aortic sinuses. The right coronary artery originates from the right sinus of Valsalva; the left coronary artery arises from the left sinus of Valsalva. The right coronary artery goes directly into the right coronary groove; the left coronary artery is short and splits into 2 branches: the left anterior descending artery and the circumflex artery. In our observation, both left and right main stems were short, with an average length of 5–7 mm (Fig. 1A).

In this study, the mean diameter of the left coronary ostium was 5 ± 0.5 mm, and the mean diameter of the right coronary ostium was 4.7 ± 0.5 mm (in the human heart: 4.8 ± 0.5 mm and

3.7 ± 0.9 mm). The distance from the right coronary artery ostium to the nadir of the annulus is much shorter than that from the left coronary artery. The main distance is 14 ± 2.4 mm in the right coronary artery (in humans: 15.4 ± 1.7 mm) and 8 ± 1.5 mm in the left coronary artery (in humans: 14.7 ± 1.3 mm). The specimens featured a muscle ridge, a post-mortem phenomenon, under the ostium of the right coronary artery, which is different from the left coronary artery and non-coronary sinus (Fig. 2).

All parameters of the aortic root, ascending aorta and aortic arch measured in the 8 dissected non-pressurized porcine hearts are summarized in Table 1. For comparison with *in vivo* dimensions, the aortic annulus was prospectively measured in 6 previous porcine experiments with transvenous intracardiac ultrasound (Siemens Acuson using a 10-Fr AcuNav ultrasound catheter) and accounted for 25.8 ± 2.5 mm. This result is somewhat greater than the 20 ± 1.2 mm found in the non-pressurized porcine root post-mortem, but it is closer to the values found for humans, i.e. 23 ± 2.5 mm. Therefore, the anatomy of the aortic root in the porcine heart is similar to that in the human heart, but there are some differences. The main anatomical features of the human aortic root and ascending aorta derived from

published echocardiographic and computed tomography scan data are shown in Table 2 [4–14].

DISCUSSION

Because of the complex anatomy and physiology of the ascending aorta, the endovascular treatment of this anatomical part is more challenging than the transcatheter endovascular treatment of the aortic arch, descending thoracic aorta and abdominal aorta. For now, with the technology available, only isolated aortic diseases located between the STJ and the origin of the innominate artery (without aortic valve and aortic root involvement) may be treated with the endovascular graft technique. In fact, in our previous study of 67 reported cases worldwide, we showed that the endovascular aortic graft was located mainly in the ascending

aorta between the coronary ostia and the innominate artery [2]. In 7 patients, the origin of the innominate artery, the left common carotid artery or the left subclavian artery was covered by the graft. The major issue was the absence of specifically designed stent graft devices developed to address the diseased ascending aorta: Currently available stent grafts for endovascular treatment of the ascending aorta are, in fact, thoracic aorta endografts, which do not fulfil the requirements for placement in the ascending aorta. They are too long to be deployed between the coronary arteries and the innominate artery. Therefore, many surgeons need to shorten the thoracic endografts while the patient is on the operating table before deploying them into the ascending aorta [15–17].

More and more elderly patients may also suffer from concomitant aortic valve disease and aortic root aneurysm or ascending aorta dilation. Therefore, as long as the aortic root and the aortic valve are both simultaneously involved, repairing the ascending aorta with a commercially available stent graft alone is not enough because the device must cover the aortic root, which, by definition, includes the valve. A single endovascular device (a 'composite-graft' implant) for combined simultaneous aortic valve replacement and ascending aorta replacement needs to be developed [18].

The convention that the porcine heart is virtually anatomically identical to the human heart is widely accepted, and it has been used as a model for the evaluation of the endovascular treatment of the ascending aorta. Wipper *et al.* [19] compared the technical feasibility and haemodynamic alterations of antegrade transcatheter access versus conventional transfemoral access for endovascular treatment of the ascending aorta in a porcine model. They concluded that the transapical access appeared technically easier, but these models were all limited to the ascending aorta without involvement of the aortic root and valve. The design and manufacturing challenges inherent in treating the diseases of the aortic root are much more complicated than simply making shorter endografts, longer cuffs or altering the nose cones of currently available devices. The anatomical and physiological complexities of the aortic root are very different from those of the ascending or descending aorta. To extend the proximal landing zone to the aortic root and the aortic valve annulus, device alterations are

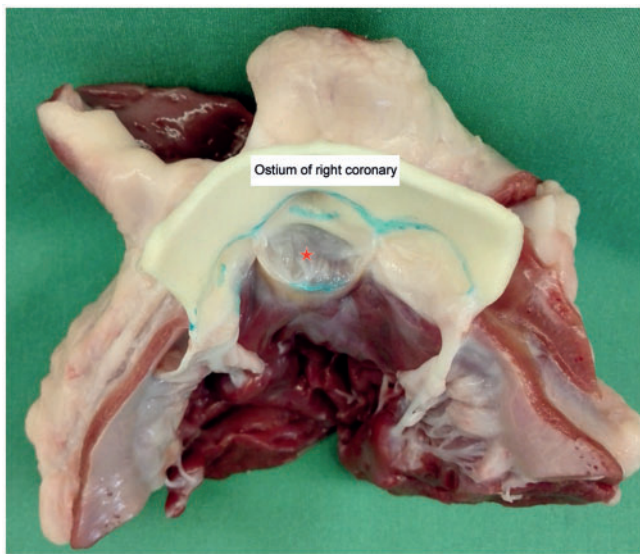


Figure 2: The right coronary sinus. The ★ shows the muscle ridge, a post-mortem phenomenon under the ostia of the right coronary artery.

Table 1: Measured anatomical parameters of the aortic root, ascending aorta and aortic arch in 8 porcine hearts

Porcine heart	BW (kg)	HW (g)	AD (mm)	SD (mm)	LCAD (mm)	RCAD (mm)	STJD (mm)	AAD (mm)	IAD (mm)	ARD (mm)	LC-LA (mm)	RC-RA (mm)	IA-LA (mm)	IA-RA (mm)	SC-A (mm)
Heart 1	89	330	19.1	20.1	5	4.5	18.8	18.2	8.5	15	6	14	43	39	29
Heart 2	88	320	20.1	20.7	6	4	19.7	17.5	8	16	7	19	47	44	36
Heart 3	99	450	19.8	20.4	4.5	5	19.1	18.2	8	15	10	17	51	47	35
Heart 4	91	360	20.1	20.7	5.5	5	20.1	18.5	7.5	14	10	14	41	38	27
Heart 5	87.5	350	20.1	20.5	4.5	5	19.9	19.6	9	15	7	13.5	45	44	39.5
Heart 6	89	400	22.6	21.3	5	4.5	21.3	19.4	9.5	14	7	12	39	37	39
Heart 7	89.5	360	20.7	21	5	5.5	20.9	20.1	8.5	15.5	8	14	46	44	41
Heart 8	79	320	18.5	19.8	5	4	19	19	9	15	7	12	38.5	36.5	35
Total	89 ± 5.4	361 ± 44.5	20 ± 1.2	20.5 ± 0.5	5 ± 0.5	4.7 ± 0.5	20 ± 0.9	19 ± 0.7	8.5 ± 0.7	15 ± 0.7	8 ± 1.5	14 ± 2.4	44 ± 4.3	41 ± 4	35 ± 4.9

AAD: ascending aorta diameter; AD: annulus diameter; ARD: arch diameter; BW: body weight; HW: heart weight; IA-LA: the distance from the ostia of the innominate artery to the nadir of the left annulus; IA-RA: the distance from the ostia of the innominate artery to the nadir of the right annulus; IAD: innominate artery diameter; LC-LA: the distance from the left coronary ostia to the nadir of the left annulus; LCAD: left coronary artery diameter; RC-RA: the distance from the right coronary ostia to the nadir of the right annulus; RCAD: right coronary artery diameter; SC-A: the distance from the start of the small curvature of the arch to the nadir of the annulus; SD: sinuses diameter; STJD: sinotubular junction diameter.

Table 2: Data of human aortic roots from previous studies

Author	Year	Object	n	Age (years)	Gender	Method	AAD (mm)	STJ (mm)	SD (mm)	AD (mm)	RCAD (mm)	LCAD (mm)	LC-LA (mm)	RC-RA (mm)
Bierbach <i>et al.</i> [4]	2010	Healthy volunteer	100	33.8 ± 14 (19–76)	M and F	TTE		25 ± 3.7 (16–36.6)	28.5 ± 3.5 (21.1–40)	21 ± 2.8 (13.5–30.6)				
Babae Bigi <i>et al.</i> [5]	2007	Health	128	21.6 ± 3.3	M	TTE	31 ± 2.9	29.5 ± 3.1	31.6 ± 3.2	21.8 ± 2.4				
D’Andrea <i>et al.</i> [6]	2010	Athletes	615	28.4 ± 10.2 (18–40)	M = 410	TTE	33 (28–39)	31 (26–37)	33 (28–42)	23 (18–28)				
Otani <i>et al.</i> [7]	2010	Normal subjects	80	70 ± 10	M = 43	TOE				25 ± 2.2 (max) 19.1 ± 1.8 (min)				
Akhtar <i>et al.</i> [8]	2009	Elderly control	25	76 ± 6.7	M = 12	CT	32.2 ± 5.8	28.2 ± 4.7	36.7 ± 5.3	27.2 ± 4.0			13.4 ± 2.0	17.6 ± 2.8
Boraita <i>et al.</i> [9]	2016	Healthy elite athletes	3281	23.1 ± 5.7	M = 2039	TTE	26.8 ± 3.6 23.5 ± 3.1	26.4 ± 3.3 23 ± 2.7	31.6 ± 3.5 27.2 ± 2.8	25.4 ± 3.2 21.6 ± 2.7				
Wendt <i>et al.</i> [10]	2013	AS patients	60	72.7 ± 8.6	M = 35	Direct vision CT (15)							14.7 ± 3.9 12.8 ± 3.5 15.3 ± 3.1	13.4 ± 4.0 13.9 ± 4.0 17.0 ± 3.6
Knight <i>et al.</i> [11]	2009	Non-CAD cadaver	150	60.4 ± 12.0 (29–86)	M = 92	CT direct vision				23.0 ± 3.8				
			75	>40	M = na									
Hamirani <i>et al.</i> [12]	2013	Chest pain	140	57 ± 10	M = 81	MDCT					4.66 ± 1.08	5.67 ± 1.18	16.0 ± 3.6	14.9 ± 4.3
Dodge <i>et al.</i> [13]	1992	Normal	20	41 ± 12	M	Coronary angiogram					3.9 ± 0.6	4.5 ± 0.5		
Leung <i>et al.</i> [14]	1991	Subjects or donor	94	15–74	M	Coronary angiogram					2.24 ± 0.55 3.65 ± 0.48 4.26 ± 0.44	4.48 ± 0.55 4.45 ± 0.31 4.85 ± 0.38		
Total		subjects	4543	48.4 ± 21.2			29.3 ± 4	27.2 ± 3.0	31.4 ± 3.4	23.0 ± 2.5	3.7 ± 0.9	4.8 ± 0.5	14.7 ± 1.3	15.4 ± 1.7

AAD: ascending aorta diameter; AD: annulus diameter; AS: aortic stenosis; CAD: coronary artery disease; CT: computed tomography; F: female; LC-LA: the distance from the left coronary ostia to the nadir of the left annulus; LCAD: left coronary artery diameter; M: male; MDCT: multidetector computed tomography; RC-RA: the distance from the right coronary ostia to the nadir of the right annulus; RCAD: right coronary artery diameter; TOE: transoesophageal echocardiography; TTE: transthoracic echocardiography; SD: sinus diameter; STJD: sinotubular junction diameter.

essential to address the problems of valve performance and coronary perfusion.

We dissected porcine aortic roots, which included the ascending aorta and the arch, and we measured their anatomical characteristics. From the dissection, we were able to confirm that the anatomy of the porcine aortic root is indeed similar to that of the human heart, which encompasses 4 anatomical structures: the aortic annulus, aortic cusps, aortic sinuses (sinuses of Valsalva) and the STJ. At the same time, when designing new devices for the root, we realized that we needed to consider some special features that would have to be tested first in pigs. For example, during percutaneous aortic root replacement, the coronary artery flow must be guaranteed because, if not, catastrophic consequences can occur in case of ostial obstruction. The location of the coronary artery noted in this study emphasizes the importance of considering such variations in the development of new devices. From this study, we know that the distance between the coronary ostia and the nadir of the annulus is extremely short, especially in the left coronary sinus, where the average distance was 8 mm compared to 14.7 mm in humans. The length of the ascending aorta was also short. The distance from the origin of the innominate artery to the nadir of the right coronary sinus was 41 mm and that to the right coronary orifice, 27 mm. Moreover, both main coronary arteries were rather short before splitting into the branches. Another important finding was that the depth of the right coronary sinus was about 5.5–6.5 mm. These anatomical characteristics are crucial for the design of a suitable device for percutaneous aortic root replacement that should be tested, at first, in animals.

Limitations

In this study, the measurements were performed under non-pressurized, static conditions, which differ from those used in the *in vivo* analyses. In particular, the corresponding human data were obtained *in vivo* from echocardiograms or computed tomography scans, whereas the pig data were collected post-mortem. The lack of a pressurized system might also explain some difference in dimensions such as the diameters of the aortic root and of the sinus of Valsalva. We learned from a previous study that an undersizing of approximately 10% is needed. This and other dimensional differences can be taken into account in the design of a suitable device and do not limit the testing of transcatheter aortic root repair.

Impact on daily practice

The goal of the present study was to validate the use of porcine aortic roots for the development of new transcatheter devices designed for the simultaneous treatment of diseased aortic valves and diseased or dilated aortic roots. The future clinical development of this technology will therefore also be based on the findings of this study. Transcatheter aortic root replacement represents a further step towards the treatment of valve and aortic diseases in elderly patients at high risk for standard surgery.

CONCLUSION

The porcine aorta model is suitable for the assessment of catheter-based aortic root repair. However, the dimensions of a root replacement device must be at the lower end of the range for clinical devices. Special attention must be given to the origin of the lower coronary artery and the configuration of the aortic arch in the porcine setting. We suggest that testing of future devices for combined aortic valve and aortic root replacement must be based on the measured distances and diameters obtained in the pig.

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Conflict of interest: none declared.

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